REMARKS

This document preliminary amends Patent Application no 10/064,392 electronically filed today, July 9, 2002. Amendments to the specification are presented in order to further clarify aspects of particular embodiments presented. No new matter has been added. A marked up version of the amendments showing changes made is provided in the attached Appendix A, below.

CONCLUSION

The Applicant submits that all pending claims are in condition for allowance. If the Examiner believes a telephone conference would expedite prosecution of this application, a telephone call to the Applicant's representative, Clifford Perry, is invited.

Respectfully submitted,

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Appendix A

Marked Up version of Amendments Showing Changes Made

Deletions are indicated by ~~strikethrough~~ and additions are indicated by <u>underlining</u>.

[0052] The electronic embodiments of these structures are capable of addressing and conveying signals to very small spatial regions, as well as to create topologically complex circuits of very high density. Application of micro-fabrication techniques has enabled the capture and management of very small fluid samples in microfluidic structures, in which both dissolved and non-dissolved biologic and chemical constituents may be manipulated In such an environment, ~~active transport and passive diffusion (collectively referred to as diffusion) of dissolved molecules and other structures~~ <u>diffusion of the biochemical species</u> can be detected, simulated, modeled, controlled, and monitored in a highly reproducible way. The transport of constituents in these systems, the way in which compounds move from one region to another depends on the activities of active components of such systems, as well as the geometries of the systems. By creating well controlled and easily simulated environments for diffusion to occur, and monitoring these processes, one can obtain a depth of understanding about the behavior of a whole range of biologic, chemical, and molecular systems.

[0055] Diffusion refers to a process by which some quantity, either matter or energy<u>, and specifically, the source constituent in the present invention</u>, moves from one location to another, usually via some prescribed thermodynamic properties such as temperature and concentration, as well as geometric properties such as length and cross-sectional area. As is well-known in the art, the basic equations governing diffusion processes are:

[0075] Diffusion occurs between a source constituent and a sink constituent which are in fluid communication with each other. <u>In one embodiment, an example of which is shown and described in Fig. 2 below, the sink constituent is located outside of the diffusion channel. In another embodiment, an example of which is shown and described below in</u> ~~The~~ <u>Fig. 8, the sink</u>

constituent is located within the diffusion channel In both embodiments, the source constituent moves toward the sink constituent through the ~~finite volume~~ diffusion channel, producing a concentration gradient which can be detected and/or measured Based upon the biologic or chemical structure of the sink constituent, the presence or absence of the source constituent's diffusion rate toward the sink constituent, and/or the rate of that diffusion, the activity of the source constitute can be ascertained. Analogously, knowledge of the biologic or chemical makeup of the source constituent and the aforementioned presence (or absence) and source constituent's rate of diffusion, conclusions as to the activity of the sink constituent can be made.

[0104] Next at 406, the channel's cross-sectional area A between measurement points z_1 and z_2 is determined. This quantity may either be known from the fabrication specifications of the channel or measured (for example, though the use of a solution with known diffusion properties and concentrations, applied to the system described) if the dimensions are not known. In an alternative embodiment, either of the other three variables may be determined if the remaining variables are known. This embodiment is discussed below with regards to calibration.

[0162] Initially, a small reaction vessel is provided. The reaction vessel meets the previously-described criteria of a finite volume diffusion channel, i.e., the volume of the reaction vessel is not greater than ~~10,000~~ 2000 times the aggregate displaced volume of the ~~source constituent to be supplied to the vessel~~ sink constituent. The reaction vessel also includes two or more measurement probes configured to detect/measure the diffusion of the source constituent, through the measurement of an electrical parameter, such as ~~conductivity~~ conductance.

[0163] Next, a cell population having a known, particular pathway is selected for study. As an example, cell populations having particular sodium ion channel behavior is selected. Subsequently, a viable and active population of the desired cells is established within the vessel, perhaps using buffers which are known to support the viability and functionality of the cell population. ~~The conductivity of~~ A baseline response of the system is obtained by measuring the conductance of the system (cells + buffer) ~~is then measured before stimulation, thereby~~

~~establishing a baseline value~~ before stimulation at two positions along the vessels height by means of two measurement probes.